

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

Claim 1 (Currently amended): An isolated heterodimeric receptor, which wherein said receptor comprises an first opioid receptor subunit and a second G-protein coupled receptor (GPCR) subunit, and wherein both receptor subunits are expressed endogenously in the same type of cell.

Claim 2 (Currently amended): The heterodimeric receptor of claim 1, wherein the second receptor subunit is an opioid receptor protein that is distinct from the first opioid receptor subunit protein.

Claim 3 (Currently amended): The heterodimeric receptor of claim 1, wherein the second receptor subunit is a dopamine receptor protein.

Claim 4 (Currently amended): The heterodimeric receptor of claim 1, wherein the second receptor subunit is an adrenergic receptor protein.

Claim 5 (Currently amended): The heterodimeric receptor of claim 1, wherein the second receptor subunit is a chemokine receptor protein.

Claim 6 (Currently amended): The heterodimeric receptor of claim 1, wherein the opioid receptor subunit is a delta opioid receptor protein and the second receptor subunit is

Serial No.: 10/018,200
Filed: January 23, 2002
Group Art Unit: 1647

selected from the group consisting of kappa opioid receptor protein, mu opioid receptor protein, D2 dopamine receptor protein, and β 2-adrenergic receptor protein.

Claim 7 (Currently amended): The heterodimeric receptor of claim 1, wherein the opioid receptor subunit is a kappa opioid receptor protein and the second receptor subunit is selected from the group consisting of delta opioid receptor protein, D2 dopamine receptor protein, α 2-adrenergic receptor protein, β 2-adrenergic receptor protein, CCR5 protein, and CXCR4 protein.

Claim 8 (Currently amended): The heterodimeric receptor of claim 1, wherein the opioid receptor subunit is a mu opioid receptor protein and the second receptor subunit is selected from the group consisting of delta opioid receptor protein and α 2-adrenergic receptor protein.

Claim 9 (Currently amended): The heterodimeric receptor of claim 1, wherein the opioid receptor subunit is a fusion protein comprising a sequence of a functional opioid receptor protein and a tag sequence.

Claim 10 (Currently amended): The heterodimeric receptor of claim 1, wherein the second receptor subunit is a fusion protein comprising a sequence of a functional second receptor protein and a tag sequence.

Claim 11 (Currently amended): A recombinant host cell that expresses a functional heterodimeric receptor, which wherein said receptor comprises an opioid receptor subunit expressed from an expression vector introduced into the host cell, and a second G-protein coupled receptor (GPCR) subunit expressed from an expression vector introduced into the same

host cell, wherein the host cell does not endogenously express the both receptor subunits are expressed endogenously in the same type of cell.

Claim 12 (Currently amended): The host cell of claim 11, wherein the second receptor subunit is a different opioid receptor protein or a covalently associated opioid receptor protein.

Claim 13 (Currently amended): The host cell of claim 11, wherein the second receptor subunit is a dopamine receptor protein.

Claim 14 (Currently amended): The host cell of claim 11, wherein the second receptor subunit is an adrenergic receptor protein.

Claim 15 (Currently amended): The host cell of claim 11, wherein the second receptor subunit is a chemokine receptor protein.

Claim 16 (Currently amended): The host cell of claim 11, wherein the opioid receptor subunit is a delta opioid receptor protein and the second receptor subunit is selected from the group consisting of kappa opioid receptor protein, mu opioid receptor protein, D2 dopamine receptor protein, and β2-adrenergic receptor protein.

Claim 17 (Currently amended): The host cell of claim 11, wherein the opioid receptor subunit is a kappa opioid receptor protein and the second receptor subunit is selected from the group consisting of delta opioid receptor protein, D2 dopamine receptor protein, α2-adrenergic receptor protein, β2-adrenergic receptor protein, CCR5 protein, and CXCR4 protein.

Serial No.: 10/018,200
Filed: January 23, 2002
Group Art Unit: 1647

Claim 18 (Currently amended): The host cell of claim 11, wherein the opioid receptor subunit is a mu opioid receptor protein and the second receptor subunit is selected from the group consisting of delta opioid receptor protein and α 2-adrenergic receptor protein.

Claim 19 (Currently amended): A method of screening for a compound that modulates a property of a heterodimeric receptor, which wherein said receptor comprises an opioid receptor subunit and a second G-protein coupled receptor (GPCR) subunit, wherein both receptor subunits are heterologously expressed endogenously in a host ~~the same type of~~ cell, which method comprises observing a change in a property of the heterodimeric receptor contacted with a candidate compound.

Claim 20 (Original): The method according to claim 19, wherein the heterodimeric receptor property is trafficking of the heterodimeric receptor.

Claim 21 (Original): The method according to claim 19, wherein the heterodimeric receptor property is binding affinity for a ligand.

Claim 22 (Original): The method according to claim 19, wherein the heterodimeric receptor property is activation of a signal transduction pathway.

Claim 23 (Original): The method according to claim 22, wherein the signal transduction pathway is selected from the group consisting of cAMP production and MAPK phosphorylation.

Claim 24 (Withdrawn): A bispecific, bivalent compound comprising an opioid receptor ligand bound to a second G-protein coupled receptor ligand, wherein the second receptor is expressed endogenously in a type of cell that endogenously expresses the opioid receptor.

Serial No.: 10/018,200
Filed: January 23, 2002
Group Art Unit: 1647

Claim 25 (Withdrawn): The compound of claim 24, wherein both ligands are agonists.

Claim 26 (Withdrawn): The compound of claim 24, wherein both ligands are antagonists.

Claim 27 (Withdrawn): The compound of claim 24, wherein both ligands are kappa receptor ligands.

Claim 28 (Withdrawn): The compound of claim 24, wherein the opioid receptor ligand is a kappa receptor agonist and the second receptor ligand is a delta receptor agonist.

Claim 29 (Withdrawn): A pharmaceutical composition comprising synergistically effective amounts of a ligand of a delta opioid receptor and a ligand of a second receptor selected from the group consisting of kappa opioid receptor, mu opioid receptor, D2 dopamine receptor, and β 2-adrenergic receptor.

Claim 30 (Withdrawn): A pharmaceutical composition comprising synergistically effective amounts of a ligand of a kappa opioid receptor and a ligand of a second receptor selected from the group consisting of delta opioid receptor, D2 dopamine receptor, α 2-adrenergic receptor, β 2-adrenergic receptor, CCR5, and CXCR4.

Claim 31 (Withdrawn): A pharmaceutical composition comprising synergistically effective amounts of a ligand of a mu opioid receptor and a ligand of a second receptor selected from the group consisting of delta opioid receptor and α 2-adrenergic receptor.

Serial No.: 10/018,200
Filed: January 23, 2002
Group Art Unit: 1647

Claim 32 (Withdrawn): A method of treating a disease or disorder selected from the group consisting of chronic pain, drug abuse, schizophrenia, depression, central reward pathway, HIV infection, cardiovascular disease, and hypertension, which method comprises administering a therapeutically effective dose of a compound of claim 24.

Claim 33 (Withdrawn): A method of treating a disease or disorder selected from the group consisting of chronic pain, drug abuse, schizophrenia, depression, central reward pathway, HIV infection, cardiovascular disease, and hypertension, which method comprises administering a therapeutically effective dose of a pharmaceutical composition of claim 29.

Claim 34 (Withdrawn): A method of treating a disease or disorder selected from the group consisting of chronic pain, drug abuse, schizophrenia, depression, central reward pathway, HIV infection, cardiovascular disease, and hypertension, which method comprises administering a therapeutically effective dose of a pharmaceutical composition of claim 30.

Claim 35 (Withdrawn): A method of treating a disease or disorder selected from the group consisting of chronic pain, drug abuse, schizophrenia, depression, central reward pathway, HIV infection, cardiovascular disease, and hypertension, which method comprises administering a therapeutically effective dose of a pharmaceutical composition of claim 31.